

APPENDICES

Appendix 1: Eligibility Criteria PICOS Search Terms for Studies to be Evaluated for Inclusion in the Systematic Review

Population	<ul style="list-style-type: none"> - Adults - Acute coronary syndrome - Atherosclerosis - Unstable angina - STEMI - NSTEMI - Coronary artery disease 																																		
Intervention	<ul style="list-style-type: none"> - 3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors - Atorvastatin - Fluvastatin - Pravastatin - Rosuvastatin - Simvastatin - Lipitor - Lescol - Lipostat - Crestor - Zocor 																																		
Comparator	<ul style="list-style-type: none"> - Placebo - Control 																																		
Outcomes	<ul style="list-style-type: none"> - CD4-CD25-FOXP3- - Regulatory T-cells 																																		
Study	<ul style="list-style-type: none"> - Randomised controlled trial - Controlled clinical trial - Randomised 																																		
Exclude (medications known to interact with statins)	<table border="0"> <tr> <td>- Amprenavir</td> <td>- Amiodarone</td> </tr> <tr> <td>- Atazanavir</td> <td>- Bezafibrate</td> </tr> <tr> <td>- Bosentan</td> <td>- Cholestyramine</td> </tr> <tr> <td>- Clarithromycin</td> <td>- Cimetidine</td> </tr> <tr> <td>- Ciprofibrate</td> <td>- Colestipol</td> </tr> <tr> <td>- Cyclosporin A</td> <td>- Danazol</td> </tr> <tr> <td>- Danazol</td> <td>- Digoxin</td> </tr> <tr> <td>- Eslicarbazepine acetate</td> <td>- Erythromycin</td> </tr> <tr> <td>- Gemfibrozil</td> <td>- Itraconazole</td> </tr> <tr> <td>- Ketoconazole</td> <td>- Linagliptin</td> </tr> <tr> <td>- Lopinovir</td> <td>- Mibefradil</td> </tr> <tr> <td>- Nicotinic acid</td> <td>- Pectin</td> </tr> <tr> <td>- Pioglitazone</td> <td>- Repaglinide</td> </tr> <tr> <td>- Ritonavir</td> <td>- Silymarin</td> </tr> <tr> <td>- Simeprevir</td> <td>- Telithromycin</td> </tr> <tr> <td>- Ticagrelor</td> <td>- Tocilizumab</td> </tr> <tr> <td>- Voriconazole</td> <td>- Warfarin</td> </tr> </table>	- Amprenavir	- Amiodarone	- Atazanavir	- Bezafibrate	- Bosentan	- Cholestyramine	- Clarithromycin	- Cimetidine	- Ciprofibrate	- Colestipol	- Cyclosporin A	- Danazol	- Danazol	- Digoxin	- Eslicarbazepine acetate	- Erythromycin	- Gemfibrozil	- Itraconazole	- Ketoconazole	- Linagliptin	- Lopinovir	- Mibefradil	- Nicotinic acid	- Pectin	- Pioglitazone	- Repaglinide	- Ritonavir	- Silymarin	- Simeprevir	- Telithromycin	- Ticagrelor	- Tocilizumab	- Voriconazole	- Warfarin
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PICOS = population, intervention, comparator, outcomes and study type; STEMI = ST-segment elevation myocardial infarction, NSTEMI = non-ST-segment elevation myocardial infarction.

Appendix 2: Process of Selecting Articles to be Reviewed

Databases	PubMed (1996 to search date) EMBASE (1947 to search date)
Search Terms	((T lymphocytes AND regulatory) OR Treg OR CD4+ OR CD25+ OR FOXP3) AND [acute coronary syndrome OR Coronary Artery Disease OR Atherosclerosis OR Myocardial Infarction OR STEMI OR ST Elevation Myocardial Infarction OR NSTEMI OR Non-ST Elevated Myocardial Infarction OR unstable angina] AND [hydroxymethylglutaryl-CoA Reductase Inhibitors OR HMGCOA reductase inhibitors OR atorvastatin OR fluvastatin OR lovastatin OR pravastatin OR rosuvastatin OR simvastatin])
Search date	13 June 2017
Hits from the search (excluding repeats, n)	187
Articles discarded after reviewing title and abstracts (n)	182
Articles discarded after data retrieval (n)	1
Articles included (n)	4

Appendix 3: Risk of Bias Assessment Details

Xie et al. 2014⁵⁴		
Bias	Authors' Judgement	Rationale
<u>Selection bias</u> Random sequence generation	Low risk	"Eligible patients were randomly assigned to control group..." p-value of relevant measurements demonstrated no difference between groups
<u>Selection bias</u> Allocation concealment	Unclear	Not described
<u>Performance bias</u> Blinding of participants and personnel	High risk	No blinding in allocation of treatment
<u>Detection bias</u> Blinding of outcome assessment	Low risk	Unlikely to affect outcome
<u>Attrition bias</u> Incomplete outcome data	Low risk	Complete data for outcomes measured, data regarding exclusions provided and number of participants provided
All markers used for Treg analysis: CD4+CD25+FOXP3+	High risk	"FITC-anti-CD4 & anti-FOXP3"
Hu et al. 2007⁵³		
Bias	Authors' Judgement	Rationale
<u>Selection bias</u> Random sequence generation	Low risk	"Patients with ACS were randomly divided into..."
<u>Selection bias</u> Allocation concealment	Unclear	Not described
<u>Performance bias</u> Blinding of participants and personnel	High risk	No blinding in allocation of treatment
<u>Detection bias</u> Blinding of outcome assessment	Low risk	Unlikely to affect outcome
<u>Attrition bias</u> Incomplete outcome data	Low risk	Complete data for outcomes measured, data regarding exclusions provided and number of participants provided
All markers used for Treg analysis: CD4-CD25-FOXP3-	High risk	"FITC-anti-CD4 & PE-anti-CD25"
Wang et al. 2015⁵²		
Bias	Authors Judgement	Rationale
<u>Selection bias</u> Random sequence generation	Low risk	"Patients were randomly divided"
<u>Selection bias</u> Allocation concealment	Unclear	Not described
<u>Performance bias</u> Blinding of participants and personnel	High risk	No blinding in allocation of treatment
<u>Detection bias</u> Blinding of outcome assessment	Low risk	Unlikely to affect outcome
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Zhang et al. 2011⁵¹		
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